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DATE: Friday, April 16, 2004

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		<i>DB=PGPB,USPT,EPAB,JPAB,DWPI; PLUR=YES; OP=ADJ</i>	
<input type="checkbox"/>	L6	L1 SAME L5	5
<input type="checkbox"/>	L5	(PROMOT\$4 OR MODULAT\$4 OR ENCOURAG\$6) NEAR10 DIFFERENTIAT\$5	11404
<input type="checkbox"/>	L4	COLON ADENOCARCINOMA NEAR10 L1	1
<input type="checkbox"/>	L3	DIFFERENTIAT\$4L2	0
<input type="checkbox"/>	L2	COLON ADENOCARCINOMA AND L1	57
<input type="checkbox"/>	L1	BILIN OR BILIVERDIN\$3 OR BILIRUBIN\$3	5877

END OF SEARCH HISTORY

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- ☐ 1. 20020169201. 13 Nov 01. 14 Nov 02. Compounds and methods for regulating cell differentiation. Falchuk, Kenneth H.. 514/422; 548/518 A61K031/4025 C07D43/14.
-
- ☐ 2. 20020099085. 15 Oct 01. 25 Jul 02. Compounds and methods for regulating cell differentiation. Falchuk, Kenneth H.. 514/422; A61K031/4025.
-
- ☐ 3. WO2003020257A. Use of beta-adrenoceptor agonists, e.g. reproterol, salmeterol or terbutaline, for restoring and/or maintaining function of damaged nerve cells, e.g. for treatment of neurodegenerative diseases. CULMSEE, C, et al. A61K031/135 A61K031/136 A61K031/167 A61K031/522 A61K045/06 A61P025/16 A61P025/28 A61K031:136 A61K031:136 A61K031:135 A61K031/522 A61K031/167 A61K031/136.
-
- ☐ 4. US20020099085A. Modulating cell proliferation or cell differentiation comprises treating a cell with a bilin. FALCHUK, K H. A61K031/4025.
-
- ☐ 5. WO 200255075A. Modulating cell proliferation or differentiation useful for the treatment of e.g. cancer involves administering bilin compounds that bind to aryl hydrocarbon receptors. FALCHUK, K H. A61K031/409 A61P007/00 A61P011/00 A61P017/00 A61P019/00 A61P021/00.
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(FILE 'HOME' ENTERED AT 15:19:39 ON 16 APR 2004)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 15:20:16 ON 16 APR 2004

L1 12460 S COLON ADENOCARCINOM?
 L2 87595 S BILIN OR BILIVERDIN? OR BILIRUBIN?
 L3 5 S L1 AND L2
 L4 35492 S (PROMOT? OR ENCOURAG? OR MODULAT?) (10A)DIFFERENTIAT?
 L5 2 S L4(10A)L2
 L6 5 S L4 AND L2
 L7 10 S L3 OR L5 OR L6
 L8 8 DUP REM L7 (2 DUPLICATES REMOVED)

=> d bib ab 1-8

L8 ANSWER 1 OF 8 MEDLINE on STN DUPLICATE 1
 AN 88080047 MEDLINE
 DN PubMed ID: 2446746
 TI **Promotion of growth and differentiation of rat ductular oval cells in primary culture.**
 AU Germain L; Noel M; Gourdeau H; Marceau N
 CS Laval University Cancer Research Center, Hotel-Dieu Hospital, Quebec, Canada.
 SO Cancer research, (1988 Jan 15) 48 (2) 368-78.
 Journal code: 2984705R. ISSN: 0008-5472.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 198802
 ED Entered STN: 19900305
 Last Updated on STN: 19970203
 Entered Medline: 19880223
 AB Oval cells emerging in rat liver at the early period of 3-methyl-4-dimethylaminoazobenzene treatment constitute a mixed epithelial cell compartment with respect to alpha-fetoprotein (AFP) and cytokeratin differential expression, and include a subpopulation which exhibits a phenotype intermediate between ductular cells and hepatocytes (Germain et al., Cancer Res., 45:673-681, 1985). In the present study we have examined the developmental potential of ductular oval cells in primary culture and after in vivo transfer. The use of monoclonal and polyclonal antibodies directed against cytokeratins of Mr 39,000 (CK39), 52,000 (CK52), and 55,000 (CK55) and vimentin, and also monoclonal antibodies against exposed surface components of oval cells (BDS7) and normal hepatocytes (HES6) allowed us to establish the ductular phenotype of the oval cells. A highly enriched preparation of oval cells was obtained by perfusion/digestion of the liver with collagenase, treatment of the cell suspension with trypsin and DNase, selective removal of hepatocytes by panning using the anti-HES6 antibody, and cell separation by isopyknic centrifugation in a Percoll gradient. The procedure yielded about 8 x 10(7) cells, of which 95% expressed CK39, CK52, and BDS7, 84% gamma-glutamyl transpeptidase, and 5% albumin and AFP. The primary response of cultured oval cells to various combinations of growth and **differentiation promoting** factors was evaluated with respect to their capacity to initiate DNA synthesis as measured by [3H]thymidine labeling from day 1 to 3, and/or to produce albumin and AFP and express tyrosine aminotransferase. Culture in the presence of either serum or clot blood extract resulted in a low proliferative activity with less than 5% of the nuclei being labeled. Over a 5-day period, fusion of a large portion of the oval cells led to multinucleated cells. When the cells were cultured in the presence of an elaborate combination of supplements [minimum essential medium containing 1 mM pyruvate, 0.2 mM aspartate, 0.2 mM serine, 1 mM tyrosine, 1 mM proline, 1 mM phenylalanine and supplemented with 20% clot blood extract, 10 ng/ml oxidized bile

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acids, 17 microM **bilirubin**, 10 ng/ml cholera toxin, 1 microM dexamethasone, 2.5 micrograms/ml insulin, 50 mM beta-mercaptoethanol, and 5 micrograms/ml transferrin (medium MX)], the labeling index increased to around 30% and the level of cell fusion greatly decreased. The addition of dimethyl sulfoxide further enhanced the initiation of DNA synthesis, while sodium butyrate acted as an inhibitor. (ABSTRACT TRUNCATED AT 400 WORDS)

L8 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 2002:539526 CAPLUS
 DN 137:88444
 TI Compounds and methods for regulating cell differentiation
 IN Falchuk, Kenneth H.
 PA Harvard College, USA
 SO PCT Int. Appl., 144 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002055075	A2	20020718	WO 2001-US47309	20011113
	WO 2002055075	A3	20031231		
	WO 2002055075	C2	20040226		
	W:		AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM		
	RW:		GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG		
	US 2002099085	A1	20020725	US 2001-977866	20011015
	EP 1404318	A2	20040407	EP 2001-998033	20011113
	R:		AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR		
PRAI	US 2000-247299P	P	20001110		
	US 2001-262233P	P	20010117		
	US 2001-264814P	P	20010129		
	US 2001-977866	A	20011015		
	US 2000-240497P	P	20001013		
	WO 2001-US47309	W	20011113		

OS MARPAT 137:88444
 AB The present invention makes available methods and reagents for inhibiting cell growth or **promoting cell differentiation** comprising contacting the cell with a differereguline such as a **bilin** in a sufficient amt. to inhibit cell proliferation or **promote cell differentiation**. The **bilin** can have cosmetic or therapeutic applications.

L8 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 2002:869588 CAPLUS
 DN 137:346170
 TI Compounds and methods for regulating cell differentiation
 IN Falchuk, Kenneth H.
 PA President & Fellows of Harvard College, USA
 SO U.S. Pat. Appl. Publ., 69 pp., Cont.-in-part of U. S. Ser. No. 977,866.
 CODEN: USXXCO
 DT Patent
 LA English
 FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002169201	A1	20021114	US 2001-8356	20011113
	US 2002099085	A1	20020725	US 2001-977866	20011015

PRAI US 2000-240497P P 20001013
 US 2000-247299P P 20001110
 US 2001-262233P P 20010117
 US 2001-264814P P 20010129
 US 2001-977866 A2 20011015

AB The invention discloses methods and reagents for inhibiting cell growth or **promoting cell differentiation** comprising contacting the cell with a differereguline in a sufficient amt. to inhibit cell proliferation or **promote cell differentiation**.

L8 ANSWER 4 OF 8 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
 on STN

AN 2003455322 EMBASE

TI The Role of Levamisole in the Adjuvant Treatment of Stage III Colon Cancer Patients: A Randomized Trial of 5-Fluorouracil and Levamisole Versus 5-Fluorouracil Alone.

AU Cascinu S.; Catalano V.; Piga A.; Mattioli R.; Marcellini M.; Pancotti A.; Bascioni R.; Torresi U.; Silva R.R.; Pieroni V.; Giorgi F.; Catalano G.; Cellerino R.

CS Prof. R. Cellerino, Clinica di Oncologia Medica, Universita degli Studi di Ancona, Ospedale di Torrette, 60020 Ancona, Italy.
 cellerin@popcsi.unian.it

SO Cancer Investigation, (2003) 21/5 (701-707).
 Refs: 19

ISSN: 0735-7907 CODEN: CINVD7

CY United States

DT Journal; Article

FS 016 Cancer

037 Drug Literature Index

038 Adverse Reactions Titles

048 Gastroenterology

LA English

SL English

AB Adjuvant 5-fluorouracil (5FU) and levamisole (Lev) have been considered standard treatment for stage III colon cancer patients. However, the uncertain contribution of Lev to the efficacy of treatment has led many oncologists to prefer the 5FU/leucovorin combination. To establish the role of Lev, we conducted a randomized trial comparing the 5FU/Lev combination with 5FU alone in patients with Dukes' C colon cancer. Patients with stage III colon cancer were randomized to receive 5FU alone (450 mg/m² IV bolus daily for 5 days and then, beginning at day 28, weekly for 48 weeks) or the same plus Lev (50 mg orally three times/day for 3 days, repeated every 2 weeks for 1 year). From December 1994 to March 1998, 92 patients were assigned to receive 5FU/Lev, and 93 were assigned to receive 5FU alone. Leukopenia and hepatic toxicity were more frequent in patients receiving 5FU/Lev as compared with those receiving 5FU (respectively, $p = 0.003$ and $p = 0.039$), whereas other toxicities were equivalent and mild in both arms. After a median follow-up time of 48 months, 80 patients have had recurrences (40 in each arm) and no advantages in terms of disease-free survival and overall survival could be demonstrated for the combination arm. The addition of Lev to 5FU does not seem to be relevant for the clinical activity of this adjuvant regimen, whereas toxicity related to Lev should be considered when an adjuvant treatment for stage III colon cancer patients is proposed.

L8 ANSWER 5 OF 8 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
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AN 2002122240 EMBASE

TI Elderly man with weakness, poor appetite, and abdominal cramping on defecation.

AU Rubin R.N.; Rubin A.M.

CS Dr. R.N. Rubin, Department of Medicine, Temple University Hospital, Philadelphia, PA, United States

SO Consultant, (2002) 42/3 (389-390).

Refs: 3

ISSN: 0010-7069 CODEN: CNSLAY

CY United States
 DT Journal; Article
 FS 016 Cancer
 020 Gerontology and Geriatrics
 037 Drug Literature Index
 048 Gastroenterology
 LA English

L8 ANSWER 6 OF 8 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
 on STN

AN 97343673 EMBASE
 DN 1997343673

TI Effect of octreotide on gastrostomy, duodenostomy, and cholecystostomy
 effluents: A physiologic study of fluid and electrolyte balance.

AU Niv Y.; Charash B.; Sperber A.D.; Oren M.

CS Dr. Y. Niv, Department of Gastroenterology, Beilinson Campus, Rabin
 Medical Center, Petah-Tikva, Israel

SO American Journal of Gastroenterology, (1997) 92/11 (2107-2111).
 Refs: 36

ISSN: 0002-9270 CODEN: AJGAAR

CY United States
 DT Journal; Article
 FS 037 Drug Literature Index
 048 Gastroenterology

LA English
 SL English

AB Objectives: Octreotide, a somatostatin analog, reduces stool and fistula
 outputs by a mechanism that is not completely understood. Our aim was to
 study its effect on gastrostomy, duodenostomy, and cholecystostomy
 effluents in a patient with colorectal cancer. Methods: Effluents of
 gastrostomy, duodenostomy, and cholecystostomy were collected in three
 separate shifts over 24-h periods beginning 3 days before octreotide
 therapy and continuing for 15 treatment days. Fifty-four samples were
 tested for volume, pH, acid, and bicarbonate production, and biochemical
 profiles. Results: A positive fluid balance was achieved immediately with
 octreotide therapy. Significant decreases in gastrostomy and duodenostomy
 outputs and in gastric acid production were observed (1433.33 \pm 33.33
 ml/24 h to 535.71 \pm 55.31 ml/24 h, $p < 0.0001$; 2066.67 \pm 66.67 ml/24
 h to 247.14 \pm 36.04 ml/24 h, $p < 0.0001$; and 67.50 \pm 3.20 mEq/h to
 13.00 \pm 1.50 mEq/h, $p < 0.0001$; respectively). Gastrostomy
 tachyphylaxis was observed after 6 days of treatment. Remarkable
 dose-dependent increases were found in cholesterol and **bilirubin**
 concentrations in the cholecystostomy effluent. Conclusions: Octreotide's
 primary effect is a decrease in gastric and pancreatic secretions. The
 increased concentrations of cholesterol and **bilirubin** may
 explain the occurrence of gallstones in patients treated with octreotide.

L8 ANSWER 7 OF 8 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
 AN 2002:519183 BIOSIS

DN PREV200200519183

TI Role of **bilirubin** in regulating colonic adenocarcinoma cell
 growth.

AU Keshavan, Pavitra [Reprint author]; Zucker, Stephen D. [Reprint author]
 CS Cincinnati, OH, USA

SO Gastroenterology, (April, 2002) Vol. 122, No. 4 Suppl. 1, pp. A-242. *for new*
 print.

Meeting Info.: Digestive Disease Week and the 103rd Annual Meeting of the
 American Gastroenterological Association. San Francisco, CA, USA. May
 19-22, 2002.

CODEN: GASTAB. ISSN: 0016-5085.

DT Conference; (Meeting)
 Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 9 Oct 2002

Last Updated on STN: 9 Oct 2002

L8 ANSWER 8 OF 8 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
 AN 1994:20937 BIOSIS
 DN PREV199497033937
 TI Biochemical modifications in the blood and the heated fluids during
 intraperitoneal chemohyperthermia.
 AU Berny, C. [Reprint author]; Mialon, A.; Manchon, M.; Le, K. E.; Panteix,
 G.; Baltassat, P.; Gilly, F. N.; Carry, P. Y.; Sayag, A.; Brailon, G.
 CS Dep. Biochem., Centre Hospitalier Lyon-Sud, F-69310 Pierre-Benite, France
 SO Oncology (Basel), (1993) Vol. 50, No. 5, pp. 362-365.
 CODEN: ONCOBS. ISSN: 0030-2414.
 DT Article
 LA English
 ED Entered STN: 25 Jan 1994
 Last Updated on STN: 25 Jan 1994
 AB The biochemical changes in blood during intraperitoneal chemohyperthermia
 (IPCH) were examined by carrying out complete assessments before and after
 the operation. These assessments were made up of 23 parameters: Na, K,
 Cl, CO-2, urea, creatinine, proteins, glucose, calcium phosphates,
 magnesium, **bilirubin**, uric acid, lactic acid, CRP, ASAT, ALAT,
 CK, LDH, gamma-GT, ALP, lipase, and amylase. Only 5 of these parameters
 showed significant changes: proteins, urea, ALP, gamma-GT, lactic acid.
 The protein and urea levels decreased due to hemodilution induced by the
 perfusion of fluids. ALP and gamma-GT levels decreased, possibly due to
 localized inhibition of secretion. Lactic acid levels increased due to
 the movement of lactates from the heated fluid into the blood. The study
 of biochemical changes within the heated fluids was made using the
 following parameters: CA 125 CA 19-9, CEA, ASAT, ALAT, CK, LDH, gamma-GT,
 ALP, lipase, uric acid, phosphates, proteins. Na, K, Cl, urea,
 creatinine, and magnesium. Between the beginning and the end of IPCH,
 significant increases were found in the levels of CA 125 (+173%), proteins
 (+190%), ASAT (+130%), LDH (+103%), K+ (+232%), PO-4 (+134%), and uric
 acid (+99%). These increases indicate the existence of a significant
 degree of cellular lysis.

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